

A PHYSIOPATHOLOGICAL STUDY OF THE
NEWBORN PIG
WITH SPECIAL REFERENCE TO
HYPOGLYCEMIA

BY

CHARLES CLEON MORRILL

D.V.M., Michigan State College, 1933

M.S., Michigan State College, 1935

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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A PHYSIOPATHOLOGICAL STUDY OF THE NEWBORN PIG WITH SPECIAL REFERENCE TO HYPOGLYCEMIA

Death of pigs during the nursing period, and particularly during the first week of life, is responsible for serious losses to swine breeders. The causes of such losses are apparently numerous, but few critical studies of the etiological factors have been made. However, Sampson, Hester and Graham have reported that certain losses observed in Illinois pigs during the first few days of life, and characterized by dullness, shivering, weakness, rough hair coat, somnolence, coma and death were accompanied consistently by hypoglycemia. They also showed that fasting of newborn pigs causes a syndrome indistinguishable from the naturally occurring disease. Madsen, Earle, Heemstra and Miller studied in Maryland rather extensive losses in young pigs due to a syndrome which in many ways resembled the condition seen in Illinois, but concluded that the cause of death was associated with uremia. This study was undertaken in an effort to further study the etiological factors involved both in the farm losses and in death from fasting of healthy newborn pigs.

Observations reported were made on 155 baby pigs farrowed at the Illinois Agricultural Experiment Station and 23 pigs with naturally occurring hypoglycemia or "baby pig disease." Of the 155 experimental pigs, 26 were sacrificed for study between 1 and 15 hours after birth, 33 were allowed to suckle their dams for 15 to 150 hours, 55 were fasted until moribund and 41 were used in experiments designed to study the influence of environmental temperature and the oral administration of fluids to the baby pig under conditions of fasting.

Included among antemortem observations were initial and final body weights and final body temperatures. After death from exsanguination, significant pathological lesions were noted and recorded and specimens collected for further laboratory examinations.

Biochemical determinations on the blood included hemoglobin by the acid hematin method, sugar by the Shaffer-Hartman-Somogyi method, non-protein nitrogen by the Koch-McMeekin

micro-Kjeldahl method, urea nitrogen by Karr's direct nesslerization method, creatinine and uric acid by Folin's methods and chlorides by the Whitehorn method. Concentration of serum calcium was determined by the Clark-Collip modification of the Kramer-Tisdall method, serum inorganic phosphorus by the Youngburg system and serum magnesium by Denis' method. On the urine, the Koch-McMeekin method was used for total nitrogen, the permutit method of Folin and Bell for ammonia nitrogen and the Folin method for uric acid. Hepatic glycogen was determined by the method of Blatherwick et al. After making an extract as described by Madsen et al, kidney uric acid values were determined by Folin's direct colorimetric method. Except for the tissue glycogen method of Blatherwick et al and the urinary uric acid method of Folin (described by Simmons and Gentskow) the foregoing methods are set forth by Koch and/or Hawk and Bergeim.

Tissues subjected to histopathological study included liver, kidney, stomach, duodenum, jejuno-ileum, pancreas, adrenal, heart, thyroid, cerebrum and hypophysis. According to the procedures desired tissues were fixed in 10 per cent formalin solution, absolute alcohol, or Zenkers, Helly's or Bouin's fixative solution made up according to Mallory. Frozen sections were made from tissues to be stained for lipoidal material. Other tissues were embedded in tissuemat and sectioned at 4 to 7 microns thickness, depending upon the tissue. Staining procedures employed included hematoxylin-eosin, Sudan IV-hematoxylin, Schultz-Schmidt and Heidenhain's aniline blue procedures according to Mallory, Gomori's chrome hematoxylin-phloxine method and Best's carmine method as modified by Chipps and Duff.

The clinical syndrome produced by fasting was indistinguishable from that of naturally occurring hypoglycemia. As hypoglycemia progressed hypothermia developed. The results of biochemical determinations on the newborn and normal pigs, fasted pigs, and clinical cases or pigs with naturally acquired hypoglycemia are summarized in Table I. Histopathological studies on these pigs revealed variations of definite significance only in the liver and kidney, although a few other characteristics of interest, but irrelevant to this problem, were noted and recorded. Sections

TABLE I

*Summary of Results of Body Fluid and Tissue Analyses,
Averages for Newborn, Control, and Fasted Pigs, and Clinical Cases.*

	Newborn Pigs	Control Pigs	Fasted Pigs	Clinical Cases
ANALYSES ON BLOOD				
Hemoglobin—gm %	10.0 (26) *	8.2 (33) *	11.5 (44) *	9.1 (22) *
Sugar—mg %	102.6 (26)	114.2 (33)	15.6 (18)	28.3 (22)
			tr (27)	
NPN—mg %	44.6 (26)	66.4 (33)	81.4 (44)	109.9 (22)
Urea N—mg %	22.3 (26)	30.8 (33)	48.4 (43)	65.8 (20)
Creatinine—mg %	2.3 (25)	1.5 (33)	1.7 (43)	2.0 (21)
Uric Acid—mg %	1.4 (26)	0.8 (33)	1.4 (44)	2.5 (21)
Chlorides—mg %	476.2 (13)	485.1 (23)	482.0 (29)	483.6 (11)
ANALYSES ON SERUM				
Calcium—mg %	10.6 (25)	12.0 (33)	10.3 (39)	11.1 (19)
Inorg Phosphorus—mg %	7.4 (19)	7.4 (27)	9.0 (18)	6.6 (15)
Magnesium—mg %	2.2 (15)	2.5 (13)	3.1 (15)	2.5 (3)
ANALYSES ON URINE				
Total Nitrogen—mg %	494.4 (8)	1038.9 (22)	1017.4 (23)	1156.1 (15)
Ammonia Nitrogen—mg %	54.8 (4)	50.8 (14)	97.4 (12)	53.8 (11)
Uric Acid—mg %	29.4 (7)	21.0 (22)	65.0 (23)	191.5 (15)
ANALYSES ON TISSUES				
Liver Glycogen—%	5.2 (14)	2.7 (26)	tr (25)	tr (18)
Kidney Uric Acid—mg/100 gm	5.2 (9)	4.0 (28)	11.8 (31)	36.7 (20)

* Denotes number of pigs on which determinations were made.
tr = trace.

from the livers of fasted pigs and pigs with naturally acquired hypoglycemia revealed complete exhaustion of glycogen as measured by histological methods while those from the livers of newborn pigs and pigs left with the sows showed glycogen present in varying amounts not too well correlated with results of chemical analysis. Among 19 cases of naturally acquired hypoglycemia 15 showed some degree of lipoidal change in the liver, a condition not observed in the other groups. This finding suggests the possibility of a complicating factor or factors in the pathogenesis of the naturally occurring disease. This possibility is further suggested by the presence of similar changes in the epithelium of the convoluted tubules of kidneys in 16 of 19 pigs with naturally occurring hypoglycemia. Although varying amounts of urates were observed both macroscopically and histopathologically in the kidneys of some fasted pigs and some pigs with the naturally acquired disease, no clinical nor histopathological evidence of obstruction or significant kidney dysfunction was observed.

Sections of porcine pancreas were difficult to obtain at 4 microns thickness, and even these proved too thick for wholly satisfactory demonstration of secretory granules in the islet cells under the conditions of this study.

Pigs fasted at an environmental temperature of 15 ± 1 degrees Centigrade survived an average of only 23.5 hours, while pigs fasted at 31 ± 3 degrees Centigrade survived an average of 83.5 hours. Pigs given distilled water or physiological saline solution by mouth developed hypoglycemia and its attendant symptoms as readily under conditions of fasting as those receiving no fluids. However, the oral administration of 50 per cent dextrose solution by mouth to otherwise fasted pigs tended to prevent the development of hypoglycemia, the exhaustion of hepatic glycogen and the development of all the symptoms of hypoglycemia except loss of body weight.

It may be concluded from this study that the normal newborn pig has an appreciable reserve of carbohydrate as indicated by the results of chemical determination of blood sugar and hepatic glycogen concentrations. Under conditions of fasting the hepatic glycogen is rapidly depleted and hypoglycemia readily develops

with its attendant symptoms of dullness, shivering, weakness, rough hair coat, somnolence, hypothermia, loss of body weight and coma. The degree of hypothermia evidently varies directly with the intensity of hypoglycemia. The rapidity with which hypoglycemia develops is influenced rather strikingly by environmental temperature, the required time varying directly with the temperature. Therefore, the practice of furnishing artificial heat by means of brooders, particularly during cold, damp weather, greatly increases the chances of survival of newborn pigs whose dams manifest transient agalactia.

Hypoglycemia in newborn pigs, whether spontaneous (naturally occurring) or experimentally produced, is accompanied by marked depletion of hepatic glycogen, moderate increase in non-protein nitrogen and urea nitrogen concentrations of the blood, possibly a slight increase of inorganic phosphorus and magnesium in the blood and often a moderate increase in uric acid content of the kidney. Results of histopathological examinations as carried out in this study furnish support for the hypothesis that the experimental syndrome observed is due primarily to hypoglycemia. This support is chiefly embodied in the histological demonstration of depletion of hepatic glycogen and lack of evidence of significant urinary obstruction in the kidneys of fasted pigs. These findings, when considered in the light of observations on human infants and the fact that apparently normal micturition was frequently observed in fasted pigs, suggest that there was no significant disturbance of kidney function, and that the observed increase in concentration of blood non-protein nitrogenous compounds represents a pre-renal azotemia, associated with protein catabolism and dehydration, rather than true uremia. This conception is further supported by a limited number of trials (6) in which oral administration of dextrose solution to otherwise fasted pigs tended to maintain normal concentrations of blood sugar, blood non-protein nitrogen and liver glycogen and to prevent development of clinical symptoms which characterize hypoglycemia except loss of body weight. Oral administration of distilled water or of physiological saline solution in a comparable number of trials (7 each) failed to prevent development of hypoglycemia or any of its clinical symptoms.

The striking resemblance of certain cases of naturally occurring hypoglycemia of newborn pigs to cases of hypoglycemia induced by fasting suggests that the naturally acquired disease may be due either to lack of nutrients or to inability to use ingested nutrients because of a disturbance of normal digestive processes. However, the possibility of the existence of some complicating factor or factors in certain cases in which duration of the syndrome is extended is suggested by the histopathological demonstration of fatty metamorphoses in varying degree and extent in the livers and kidneys.

Histopathological determination of certain substances such as glycogen and uric acid in tissues is only roughly quantitative and should not be relied upon to demonstrate lesser concentrations of such substances. Furthermore, for adequate demonstration of cytological detail in the islets of Langerhans, sections of porcine pancreas should be less than 4 microns in thickness and perhaps as thin as 2 microns.

Further research is needed for the full understanding of etiological factors involved in certain naturally occurring cases of hypoglycemia in young pigs. Use of the nonspecific term "baby pig disease" should be avoided whenever possible, particularly when the etiological factors are known.

BIBLIOGRAPHY

- Blatherwick, N. R., P. J. Bradshaw, M. E. Ewing, H. W. Larson and S. D. Sawyer
1935. The determination of tissue carbohydrates. *J. Biol. Chem.* 111:537-547.
- Chippes, H. D., and G. L. Duff
1942. Glycogen infiltration of the liver cell nuclei. *Am. J. Path.* 18:645-659.
- Gomori, G.
1941. Observations with differential stains on human islets of Langerhans. *Am. J. Path.* 17:395-406.
- Hawk, P. B., and O. Bergeim
1937. *Practical physiological chemistry*, Eleventh edition. P. Blakiston's Son and Co., Philadelphia.
- Koch, F. C.
1943. *Practical methods in biochemistry*. Third edition (revised). The Williams and Wilkins Co., Baltimore.

- Madsen, L. L., I. P. Earle, L. C. Heemstra and C. O. Miller
1944. Acute uremia associated with "uric acid infarets" in the kidneys of baby pigs. *Am. J. Vet. Research* 5:262-273.
- Mallory, F. B.
1938. *Pathological technique*, W. B. Saunders Co., Philadelphia and London.
- Sampson, J., H. R. Hester and R. Graham
1942. Studies on baby pig mortality II. Further observations on acute hypoglycemia in newly born pigs (so-called baby pig disease). *J. Am. Vet. Med. Assoc.* 100:33-37.
- Simmons, J. S., and C. J. Gentskow
1944. *Laboratory methods of the United States Army*. Fifth edition; Lea and Febiger, Philadelphia.

VITA

The author was born November 20, 1907, in Laingsburg, Michigan. His secondary school education was completed at Eaton Rapids, Michigan, whereupon he matriculated at Michigan State College. He was awarded the degree, Doctor of Veterinary Medicine, in 1933. Scholarship honors for undergraduate work included prizes for highest scholastic average among freshman veterinary students, senior veterinary students and the entire graduating class of 1933. During the last three years of undergraduate study he was employed part-time as an assistant in the Department of Animal Pathology. After graduation he continued as laboratory assistant in that department and did graduate work until 1935 when he was granted the degree, Master of Science. From 1935 till 1939 he served in the Department of Pathology, Division of Veterinary Medicine, Kansas State College, first as assistant professor, then as associate professor. His duties consisted of teaching general and special veterinary pathology and participating in the diagnostic service. In 1939 he came to the University of Illinois to take up his present assignment in diagnosis and research in animal diseases in the Department of Animal Pathology. At present he holds the rank of assistant professor.

The author is a member of Alpha Psi, Phi Kappa Phi, Sigma Xi, Phi Sigma, Gamma Sigma Delta, American Veterinary Medical Association, Illinois State Veterinary Medical Association, Conference of Research Workers in Animal Diseases in North America and International Association of Medical Museums. The titles of some of the more significant of his 28 publications follow.

Morrill, C. C.

1938. A histopathological study of the bovine udder. *Cornell Vet.* 28:196-210.

Morrill, C. C.

1939. Erysipeloid: occurrence among veterinary students. *J. Infect. Diseases* 65:322-324.

Morrill, C. C., and R. Graham

1941. An outbreak of bovine pseudorabies or "mad itch." *Am. J. Vet. Research* 2:35-40.

Graham, R., N. D. Levine and C. C. Morrill

1943. Listerellosis in the domestic animals. Univ. of Ill. Bull. 499.

Graham, R., E. H. Peterson, C. C. Morrill, H. J. Hardenbrook, G. E. Whitmore and P. D. Beamer

1945. Studies on porcine enteritis. I. Sulfathalidine therapy in treatment of natural outbreaks. J. Am. Vet. Med. Assoc. 106:7-13.

Peterson, E. H., C. C. Morrill and R. Graham

1945. Embryo mortality accompanied by pasty eyes and severe losses in ducklings associated with avitaminosis. Am. J. Vet. Research 6:96-102.

